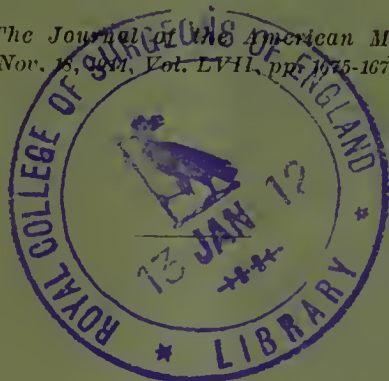


EIGHT MONTHS' EXPERIENCE WITH SALVARSAN AT THE NEW YORK SKIN AND CANCER HOSPITAL

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AND
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NEW YORK

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A few months ago we expressed some opinions on the value of salvarsan, based in part on our own experience and in part on that of others. Our present communication is a detailed account of work that has been done during the past eight months, and the conclusions drawn are based entirely on our own experience.

The greater part of our observations have been made at the New York Skin and Cancer Hospital in the service of Dr. George Henry Fox. At the time of writing, 128 injections have been given to 100 selected patients. The first ten patients were treated by the subcutaneous method (Wechselmann), after which intramuscular injections of an alkaline solution (Lesser method) were tried in twenty cases. Later, the intravenous method was employed in sixty-nine cases and intramuscular injections of an oily suspension in twenty-nine cases. The treatment was repeated in twenty-one of our patients, three of them receiving three, and two receiving four separate injections.

We have been fortunate in being able to follow a large proportion of the cases both clinically and serologically. Shortly before completing our report, we had personally observed or received letters from eighty-five of our patients. Of the remaining fifteen cases, ten had been under observation for at least a month.

Three patients with primary lesions were treated before the appearance of any general manifestations. They were unfortunately not seen at an early enough period to attempt to abort a general infection, as at the

* Read in the Section on Pharmacology and Therapeutics of the American Medical Association, at the Sixty-Second Annual Session, held at Los Angeles, June, 1911.

time of treatment the Wassermann reaction had already become positive.

Our early opinions regarding some of the cutaneous lesions of syphilis have not materially changed as a result of further experience. The macular syphilids have not disappeared with any surprising rapidity, and the papular syphilids have generally proved pretty resistant

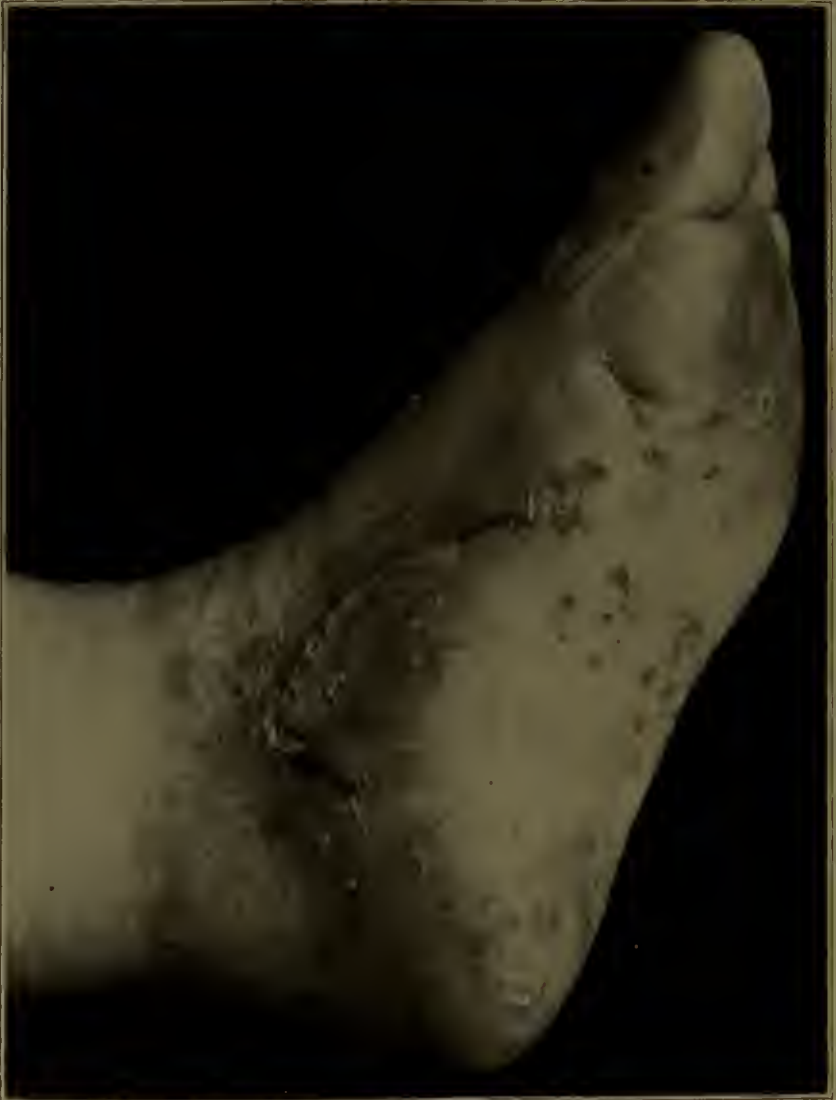


Fig. 1.—Tuberculo-squamous syphilid of twelve years' duration.

to treatment. Gummatous lesions have generally yielded to salvarsan in a most satisfactory manner, while mucous patches and condylomata have regularly disappeared in a most surprisingly short time.

In four cases (68, 74, 58 and 77) of late syphilis of the palms and soles, lesions which are notoriously resist-

ant to mercury, the results of single injections of salvarsan have been extremely gratifying. One of these patients (68) had suffered from an extensive syphilid of the sole for twelve years, in spite of a good deal of treatment with mercury by several competent syphilologists. One month after a single intramuscular injection,



Fig. 2.—Same as Fig. 1, one month after one intramuscular injection.

the eruption had completely disappeared. In the other cases, the lesions had existed for three years, two years and two months respectively and disappeared in an equally satisfactory manner. Indeed, in one case a verrucous syphilid of the palms entirely cleared up in one week after an intravenous injection.

Four of the patients suffering from early syphilis presented an iritis which disappeared at the end of three weeks. In one case the iritis became more severe after treatment and on the fourth day had involved the other eye. A most excellent result was obtained in a case (57) of syphilitic neuroretinitis in a patient who had been infected a year and a half previously. Before injection



Fig. 3.—Gummatous ulceration of six months' duration.

her vision (examined by Dr. H. H. Tyson) was 20/100 in the right and 20/70 in the left eye. At the end of sixteen days there was a decided clearing of the fundus and she could read 20/30 minus with both eyes. One week later the fundus was practically normal in appearance and the vision was 20/20 minus in the right and 20/30 minus in the left eye.

Headaches occurring in both the early and late stages of syphilis were generally very favorably affected by salvarsan. Pains accompanying early manifestations, those associated with gummatous lesions and especially with periostitis, also yielded very satisfactorily.

One patient suffering from incipient tabes was treated without any benefit. In one case of hereditary syphilis

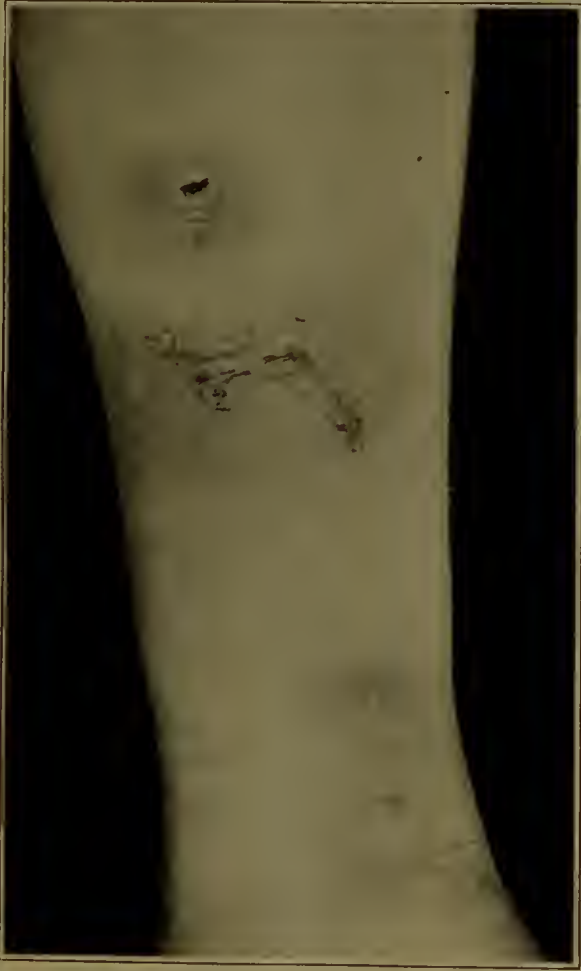


Fig. 4.—The lesions shown in Figure 3, view ten days after one intramuscular injection.

the result was excellent, in another moderately good. In a case of leukoplakia of the mouth no improvement was obtained. In a case of extensive leukoplakia of the tongue, there was a temporary lessening in the thickness of the patches, without any diminution in their extent.

The all-important question of the permanence of the action of salvarsan can hardly be fairly discussed until

a period of several years at least has elapsed. It must be said, however, that the number of relapses in our cases has been somewhat less than would have been expected as a result of our earlier experience. One of our patients relapsed repeatedly after four different injections, comprising all of the four methods of administration that we have used. Three patients relapsed after one injection and four cases after two injections had been given. Three patients relapsed or remained stationary after the first, but responded favorably to a second injection. The patients in whom failures, or at least unfavorable results were obtained, included the case of tabes and a case* (16) in which the diagnosis was in some doubt (gummatous vs. varicose ulcers). In addition, a case of gummatous ulceration of the leg showed no response to treatment at the end of three weeks, while the results in three others (38, 43 and 87) must be considered unsatisfactory. In all there were fifteen cases in which either relapse or unsatisfactory results were observed.

Many of the patients in whom excellent results were obtained by salvarsan had been previously treated by mercury without success. It is probable, however, that most of these cases at least would have yielded in a satisfactory manner to mercury if its administration had been sufficiently vigorous and thorough. An example of the very rare cases in which mercury cannot be tolerated in any form was shown by a case (83) of extensive gummatous ulceration of the palate. For eighteen months an experienced syphilologist had attempted to treat this patient by injections, inunctions and internal administration of mercury. Small doses had proved of no avail and large doses had been followed by necrosis of portions of the gums. We spoke of this case in our first communication¹ as one in which a "disappointing relapse" had occurred; we are now glad to be able to report that the ulcerations healed entirely after a second injection and that no further relapse had occurred at the end of seven months.

The Wassermann test was made in every case before treatment and subsequently as often as circumstances permitted. More than 400 examinations were made in the course of eight months. The original Wassermann

1. Fox and Trimble: THE JOURNAL A. M. A., March 4, 1911, p. 650.

TABLE 1.—PATIENTS TREATED WITH ONE SUBCUTANEOUS INJECTION

Case No.	Sex	Age	* Stage	Lesions	Duration of Lesions	Previous Treatment	Date and Dosage	Local Effect of Injection	Clinical Result. Remarks	Wassermann Reaction
1	F.	48	2	Flat papular syphilid.	Five weeks.	None.	10/13/10, gm. 0.5	Severe pain 12 hrs.; induration persists at the end of 8 mos.; no necrosis.	Eruption disappeared in 3½ months; relapse 1 month later, accompanied by severe headache; given Hg, after which lesions disappeared in a month; menses irregular but possibly due to menopause.	Negative in 11 wks. Positive at the end of 8 months.
2	F.	32	3	Tuberculo-ulcerative syphilid of face.	Two years.	Hg at irregular intervals by mouth and injections for two years; disease not controlled by mercury.	10/22/10, gm. 0.5	Severe pain 2 wks.; induration persists end 8 mos.; tender and red for first 5 mos.; no necrosis.	Nasal discharge stopped end of 1 week; lesions healed in 10 days; menses irregular since treatment; no relapse at end of 8 months.	Faintly positive at the end of 8 months.
3	F.	27	3	Gumma of clavicle; tubercular syphilid of lip.	Gumma 4 months; lip lesion 12 years.	Hg at irregular intervals for many yrs.; improved but never cured.	10/22/10, gm. 0.45	Practically no pain; necrosis 10 weeks later; not entirely healed at end of 8 months.	Gumma healed in 6 weeks; syphilid of lip disappeared in 10 days; no relapse at end of 8 months; at end of 3 weeks gained 5 pounds and looked better; since then in poor general health; menses delayed 7½ months.	Positive at the end of 8 months.
4	M.	32	2	Papulo-squamous syphilid; extensive mucous patches.	Three months.	Hg by mouth for one month.	10/28/10, gm. 0.5	Pain and induration marked; necrosis six weeks later; curetted 6 months later and still discharging at end of 7½ months.	Mucous patches disappeared in 10 days, eruptions in 2½ months; no relapse at end of 7½ months; gained 18 pounds; general appearance greatly improved.	Negative in 6 wks.; Remained at the end of 7½ months.
5	M.	37	2	Pustular syphilid.	Four months.	Hg by mouth for four mos. without effect on eruption.	10/29/10, gm. 0.5	Pain severe; induration slight.	Moderate improvement at end of 1 week, when patient left clinic; from Dr. Jerome Kingsbury we learn that lesions disappeared at end of 1 month; relapse 6 months later, consisting of a general papulo-squamous syphilid.	Negative before and after treatment.
6	M.	21	2	Maculo-papular syphilid.	Five weeks.	None.	10/29/10, gm. 0.45	Pain severe for 12 hours; induration moderate.	Slight improvement at end of 3 weeks, when patient was lost to observation.
7	M.	34	3	Tuberculo-ulcerative syphilid of arm, shoulder, abdomen; ulceration of palate.	Four months.	Hg by mouth two weeks.	11/3/10, gm. 0.5	Pain severe on second day; induration moderate.	Ulceration healed in 3 weeks; no relapse at end of 7 months.	Strongly positive at the end of 3 weeks.

* 1, primary; 2, secondary; 3, tertiary.

TABLE 2.—PATIENTS TREATED WITH ONE INTRAMUSCULAR INJECTION (ALKALINE SOLUTION)

Case No.	Sex	Age	* Stage	Lesions	Duration of Lesions	Previous Treatment	Date and Dosage	Local Effect of Injection	Clinical Result. Remarks	Wassermann Reaction
8	M.	24	2	Superficial ulceration of mouth; laryngitis.	Ten months.	None.	11/10/10, gm. 0.45	Severe pain and swelling; lameness 3 wks.; soreness in sitting for 3 mos.	Ulcers in mouth disappeared in 3 days, hoarseness improved on second day and voice normal on fifth day; no relapse at end of 7 months; gained 23 pounds.	Negative in 8 wks.; faintly positive at the end of 7 months.
9	F.	46	3	Serpiginous syphilid of face.	One year.	None.	11/15/10, gm. 0.5	Severe pain and induration; lameness 3 weeks; in bed 2 weeks.	Eruption entirely well at end of 1 month; no relapse at end of 7 months.	Weakly positive in 8 weeks; strongly positive at the end of 5 months.
10	F.	36	3	Gumma of pharynx; gummatous infiltration of accessory sinuses; deafness.	Three years.	Hg by mouth 18 months.	12/3/10, gm. 0.45	Pain and induration moderate; slight necrosis at end of a week, with continual slight discharge for 6 mos.	Lesions practically healed at end of 1 month; deafness not changed; no relapse at end of 6 months; gained 19 pounds.	Faintly positive at end of 6 months.
11	M.	43	3	Tuberculo-ulcerative syphilid of thigh.	Seven months.	None.	12/5/10, gm. 0.45	Severe pain and induration for one week.	Ulceration healed at end of 3½ weeks; no relapse at end of 6 months.	Positive at the end of 6 months.
12	M.	23	2	Macular syphilid.	Ten days.	None.	1/10/11, gm. 0.6	Severe pain; tremendous swelling of buttocks; lameness for 4 weeks.	Eruption disappeared in a week; no relapse at end of 4 months; does not suffer from flatulence as much as formerly.	Faintly positive at the end of 4 months.
13	F.	23	3	Gummatous ulceration of leg.	Six months.	None.	1/12/11, gm. 0.6	Pain severe; induration moderate.	Ulceration healed at end of 10 days; no relapse at end of 5 months; menstruation irregular since injection; has gained 5 pounds.	Faintly positive at the end of 5 months.
14	F.	34	2	Maculopapular syphilid.	Three weeks.	None.	1/12/11, gm. 0.6	Pain and induration slight.	Eruption disappeared at end of 1 month; ten weeks later lritis, treated with Hg at another hospital.	Negative in 4 wks. and at end of 6 wks.
15	F.	20	2	Latent.	Hg by mouth 8 months.	1/12/11, gm. 0.6	Severe pain for three days; induration and lameness three weeks.	No manifestations at end of 5 months; has gained 15 pounds.	Negative in 5 wks.; weakly positive at end of 5 months.
16	F.	52	3	Gummatous ulceration of leg.	Four years.	None.	1/24/11, gm. 0.6	Severe pain 3 days; induration 3 wks.	Ulcers improved slightly at first, became cleaner but not much smaller; menstruation irregular since treatment (possibly menopause).	Negative at end of 4½ mos.
17	F.	34	2	Condylomata of vulva; psoriasis.	Condylomata 2 months; psoriasis 3 months.	None.	1/31/11, gm. 0.6	Severe pain 3 days; induration moderate.	Condylomata disappeared at end of 1 week; psoriasis lesions nearly well at end of 3½ months (see text); dysmenorrhea since treatment.	Negative in 12 wks. and at end of 3 mos.
18	M.	24	2	Papulosquamous syphilid.	Six weeks.	Salvarsan 1 mo. before, subcutaneously.	2/18/11, gm. 0.6	Pain two days; induration moderate.	Eruption disappeared in 3 weeks; no relapse at end of 7 weeks.	Negative in 4 weeks and at end of 5 wks.
19	M.	30	1	Chancre (spirochetes present).	Eleven days.	None.	3/1/11, gm. 0.6	Pain two days.	Chancre covered with epidermis in 6 days; induration of chancre disappeared in 1 month; no manifestations at end of 3 months.	Negative in 4 wks. and at end of 10 wks.
20	F.	24	2	Latent.	Hg by mouth and inunctions one year.	3/8/11, gm. 0.6	Severe pain and induration; in bed 2 weeks.	No manifestations at end of 3 months; lost 18 pounds, which she has not regained at end of 3 months.	Negative at end of 4 weeks.

* 1, primary; 2, secondary; 3, tertiary.

method was followed, using as antigen a reliable alcoholic extract of syphilitic liver.

The results of the Wassermann reaction may be conveniently considered in two groups, those of patients who received one and those of patients who received two or more injections. Of the patients who were treated by a single injection, seventy-one showed a positive Wassermann reaction before treatment. Of these cases, twenty-eight became negative at an average period of about six weeks. In these the reaction later became positive in two, weakly positive in three cases and faintly positive in one case. The twenty-two cases which remained negative (30 per cent.) were followed, on an average, two and a half months; some of them for six and eight months. Of the remaining forty-three cases, ten showed a temporary and twenty a final weakening in the reaction. In eleven cases the reaction remained the same. In two cases it became stronger.

Of the cases in which two or more injections were given, twenty were positive before treatment. Of these four became negative in periods varying from five to nine weeks. One of these later again became positive. Of the remaining fifteen cases five showed a temporary and eight a final weakening in the reaction, while eight remained the same. The total number of cases which remained negative after either single or multiple injections was twenty-five (27 per cent.).

In all except five of the cases ophthalmoscopic examination of the fundus was made, although we have for some time considered that such an examination was an unnecessary precaution. Routine examinations of the urine were made before and after injection and showed a transitory albuminuria in a few cases.

At the beginning of our experiments every patient was required to remain in bed for three days after treatment. More recently the patients receiving intramuscular injections of oily suspension have been allowed to go home after treatment and advised to keep as quiet as possible for several days. Patients receiving intravenous injections have been required to remain in bed only for twelve, or in some cases four or five hours.

There have fortunately been no serious ill effects from salvarsan up to the time of writing. Deafness appeared in one case three months after treatment, but was found on aural examination to be due to acute catarrhal otitis

media. The patient presented a chronic rhinitis and pharyngitis and had also suffered from a discharge from the opposite ear before the administration of salvarsan. Another patient (68) who had complained of smarting of the eyes and blurring of vision, showed no abnormal changes in the fundus on ophthalmoscopic examination.

Among the general effects of salvarsan should be mentioned a marked improvement in general health that was noted in quite a number of cases. Seventeen of our patients showed a decided gain in weight, one of them gaining 23 pounds in the course of seven months. In three cases, however, there was a loss of from 15 to 18 pounds, which had not been regained in two of the cases at the end of three months.

After subcutaneous and intramuscular (Lesser) injections the temperature rose as a rule on the second day and lasted from one to three days. In five cases there was no reaction whatever, while in the others the height of the temperature ranged from 99 to 102.6. After intravenous injections the temperature rose as a rule within a few hours, its height varying from 99 to 103. No temperatures were taken after most of the oily injections, the patients being allowed to go home immediately after the treatment.

Among the general symptoms noted after intravenous injections were chills or chilly sensations in twenty-seven cases, vomiting in twenty-five, headaches in fourteen cases. One patient complained of dizziness, another of diarrhea for a day, and two suffered from sleeplessness for several days. In twenty-eight cases there were no symptoms whatever. Two patients who had shown a marked reaction after the first injection showed no symptoms after the second had been given.

The local effects of intramuscular injections of alkaline suspensions included pain, induration and lameness, which were very severe in nine cases, moderate in five and slight in five cases. The discomfort in some of the cases was severe enough to warrant the use of morphin. After intramuscular injections of oily suspensions the local effects were severe in ten, moderate in eleven and slight in eight cases. In the worst cases the patients were obliged to remain in bed for a week or more, and even at the end of several months they complained of some stiffness about the buttocks and thighs. Necrosis occurred in two cases (3 and 4) after subcutaneous injection.

tions, in one case (10) after the intramuscular injection of an alkaline solution, and in two cases (70 and 88) after intramuscular injections of oily suspensions. At the time of writing nine of the ten patients that had been treated by the subcutaneous method still presented the characteristic indurations between the scapulae; the tenth case had been early lost to observation.

Among the interesting by-effects that were observed may be mentioned a case (85) in which a herpes zoster appeared on the trunk ten days after the injection. A general toxic erythema occurred in two cases (41 and 68) on the seventh and ninth days respectively after treatment, lasting three days and accompanied by febrile symptoms. In one case the temperature rose on the first day to 104.

Treatment with salvarsan had no disturbing effect on pregnancy in one of our cases (21) which was followed from the sixth month to full term, and in another case which could only be followed for a month.

Disturbances in menstruation were noted in twelve cases after treatment. In two of the cases the irregularities were possibly due to the menopause. In another case the cessation of the flow was probably due to pregnancy. In one case the menstrual periods became more regular, while in the others they became more irregular after injection, being delayed in one case for seven and a half months.

One patient with nodular leprosy was experimentally treated with an intramuscular injection. In our first report we stated that this patient had been prostrated by the treatment and that no benefit had resulted from the injection. A change occurred, however, a month later when numerous ulcerating lesions of the face healed entirely. Two weeks later there was a partial relapse. No change in the solid nodular lesions was noted. A small dose of salvarsan was later given intravenously without producing any improvement or indeed any reaction whatsoever.

Two patients (17 and 90) who were treated for syphilis also presented complicating lesions of psoriasis. In one case the eruption was practically well at the end of three and a half months. In the other case, in which (according to the patient's statement) the eruption had existed for forty years, there was a complete disappearance of the psoriatic patches at the end of six weeks and at the end of three months no relapse had occurred.

In giving intravenous injections we have employed the gravity method in all of our cases except the first, in which the more complicated Schreiber apparatus was tried. We have had practically no difficulty and no bad results. For most of the injections we have used our own model of the gravity apparatus described elsewhere.² In this communication we recommended the Schreiber form of needle having a 17 or 18 bore and a bevel that was not too long. Our experience with some of the short beveled and dull needles has led us to modify our views. We are now convinced that the most suitable needle is of the Schreiber type, having an 18 bore (Stubbs) and a bevel of about 3 or 4 mm., that is, not too sharp and not too dull. For diluting the salvarsan we use only sterile distilled water and dispense entirely with the salt solution. This may be the cause of the appearance of small nodules in the vein in eight out of sixty-nine injections. In two cases they were present at the last time of observation, the fourth and tenth weeks respectively after treatment. In the others they had disappeared in from one to four weeks. The simplicity of using water instead of salt solution is an advantage that in our opinion more than compensates for the appearance of some of these harmless nodules.

CONCLUSIONS

1. Salvarsan is a powerful symptomatic remedy for the treatment of syphilis.
2. It acts with greatest rapidity on lesions of the mucous membranes.
3. It is of decided value in obstinate palmar and plantar syphilids.
4. The permanence of its action cannot be determined until a number of years have elapsed.
5. Salvarsan should be used in conjunction with mercury and cannot entirely replace this valuable remedy, except in a few selected cases.
6. The effect of salvarsan on the Wassermann reaction is less favorable than on the clinical manifestations of syphilis.
7. Its effect on the Wassermann reaction is in general analogous to that of mercury.

2. Fox and Trimble: *Med. Rec.*, March 18, 1911, lxxix, p. 469.

TABLE 3.—PATIENTS TREATED WITH ONE INTRAVENOUS INJECTION

Case No.	Sex	Age	Stage	Lesions	Duration of Lesions	Previous Treatment	Date and Dosage	Local Effects of Injection	General Effects of Injection	Clinical Result	Remarks	Wassermann Reaction
21	P.	17	2	Coudylomata.	Three months.	None.	2/2/11, gm. 0.5		Chill; vomited once; abdominal pain 12 hours.	Coudylomata disappeared in 1 week; no relapse at end of 4½ months; no interference with pregnancy; baby born at full term, apparently healthy, except for scurvy.		Fatally positive at end of 4½ months.
22	M.	21	2	Mucous patches.	Eight months.	43 injections.	2/3/11, gm. 0.5		Chill, nausea; vomited once.	Mucous patches healed 12 hours after injection; headaches stopped at same time; abdominal pains and diarrhea 10 days after injection, lasting 5 days; no relapse at end of 4½ months.		Negative in 8 weeks and at end of 4 months.
23	M.	40	2	Latent.		30 inoculations.	2/7/11, gm. 0.5		Slight chill, nausea; vomited twice; headache for 12 hours.	Given Hg at end of 3 weeks.		Negative in 3 and at end of 4 weeks.
24	F.	24	3	Tuberculo-ulcerative syphilid of neck.	One month.	20 injections.	2/9/11, gm. 0.5			Lesions healed in 5 days; favorable effect on menstruation (see text); no relapse at end of 4 months; gained 17 pounds.		Weakly positive at end of 4 months.
25	F.	30	2	Latent.		None.	2/25/11, gm. 0.5		Nausea; vomited 3 times.	No new manifestations; gained 5 pounds.		Positive at end of 3½ months.
26	M.	7	†	Gumma.	Three years.	None.	2/25/11, gm. 0.2			Gumma healed in 1 month; improved in general appearance.		Positive at end of 3½ months.
27	M.	45	3	Tuberculo-squamous syphilid of forehead and scalp.	Ten weeks.	Hg by mouth intermittently for 1 year; 65 injections.	2/28/11, gm. 0.5		Headache for a few hours.	Eruption began to disappear on second day; lesions that in 2 weeks; relapse came in 8 weeks; hemorrhages and ulcers healed in 3 months; gained 8 pounds.		Negative in 7 weeks and at end of 4 months.
28	F.	26	3	Gummatous ulceration of leg.	Four months.	Hg by mouth 4 months.	3/2/11, gm. 0.5			Pain that had existed in ulcers and bones for several months disappeared on third day; ulcers did not heal and patient put on Hg treatment.		Positive at end of 5 months.
29	M.	31	3	Tuberculo-ulcerative syphilid.	Four months.	Hg intermittently 2 weeks.	3/9/11, gm. 0.5	One bean-sized nodule lasting a week.	Dizziness, chill, nausea; vomited twice.	Ulcers healed in 10 days; no relapse at end of 3 months.		Negative at end of 3 months.
30	F.	41	3	Gummatous ulceration of knee.	Two yrs.; at times temporarily healed.	None.	3/9/11, gm. 0.5			Ulcers healed in 10 days; no relapse at end of 3 months.		Weakly positive at the end of 3 mos.
31	F.	31	3	Tuberculo-ulcerative syphilid.	Five years.	Hg by mouth 1 yr.; disease not controlled by treatment.	3/11/11, gm. 0.5		Chill; vomited twice.	Ulcers healed at end of 2 weeks; menstruation delayed few days for first three periods; no relapse at end of 3 months.		Negative in 8 weeks and at end of 3 months.
32	F.	21	2	Maculo-papular syphilid.	Two weeks.	None.	3/11/11, gm. 0.5	Slight pain in arm for 12 hours.		Eruption entirely disappeared in 5 wks.; no relapse at end of 2½ months; lost 15 pounds; given mercury at own request.		Negative at end of 8 weeks.
33	F.	20	2	Papular syphilid.	Four months.	Hg by mouth 2 weeks.	3/14/11, gm. 0.5		Slight nausea and headache.	Lesions healed in 3 weeks; felt "stiff all over" for six weeks following injection.		Weakly positive at end of 3 months.
34	M.	28	2	Small flat papular syphilid.	Three weeks.	None.	3/16/11, gm. 0.5		Chill lasting thirty minutes.	Papules dried up in 3 days; papules flattened and chancres hardly visible at end of 2 weeks; end of 1 month only staining remained from eruption; no relapse at end of 3 months; gained 8 pounds.		Negative at end of 3 months.
35	M.	61	3	Gummatous ulceration of leg.	Six years; never entirely healed.	None.	3/23/11, gm. 0.5			Ulcers (25 in number) entirely healed at end of 1 month, with exception of 1 bean-sized lesion; no relapse at end of 2½ months; gained 6 pounds.		Weakly positive at end of 2½ mos.
36	F.	30	2	Miliary papular syphilid.	Three weeks.	None.	3/23/11, gm. 0.5		Slight headache on following night.	Stiffness of knee disappeared on second day; eruption was slowly disappearing at end of 2 weeks, when patient left the clinic.		
37	F.	23	3	Gummatous ulceration of soft palate.	One year.	Hg by mouth 4 years.	3/25/11, gm. 0.5	One pea-sized nodule disappeared in 2½ weeks; no obliteration of vein.	Chill and slight headache.	Lesions healed in 4 weeks; swallowing became much easier on third day and normal at end of 1 week; menses stopped, probably due to pregnancy.		Fatally positive at end of 2½ mos.
38	M.	23	3	Tuberculo-ulcerative syphilid.	One year.	None.	3/26/11, gm. 0.5	Two nodules, which disappeared in one month.	Chills, nausea, vomiting three times; severe headache.	Tubercles of face flattened in 3 weeks; three out of five ulcers of leg healed in 3 weeks and remained healed 2½ mos.; other 2 ulcers did not heal.		Weakly positive at end of 2½ mos.
39	M.	43	3	Disappearing gumma of liver.	Eighteen months.	Hg by mouth for 18 mos., given 12 times and again 18 mos. ago.	3/26/11, gm. 0.5	Pea-sized nodule present at end of 10 weeks.	Chill, nausea; vomited three times; headache and dizziness.	Tenderness over liver disappeared day after injection; relief of chronic constipation; great improvement in appetite and general health.		Positive at the end of 10 weeks.
40	M.	28	2	Latent.		Hg by mouth 6 months.	3/27/11, gm. 0.5		Chill, nausea; vomited four times; diarrhea.			Negative at the end of 6 weeks.
41	F.	20	2	Macular syphilid.	Two months.	None.	3/30/11, gm. 0.5	Slight soreness of arm; one nodule disappeared in two weeks.	Chill, nausea, headache.	Eruption disappeared in a month; toxic erythema and temperature 104.8 on ninth day (see text); no relapse at end of 2½ months.		Negative at the end of 9 weeks.
42	F.	21	2	Macular syphilid.	Two weeks.	None.	3/30/11, gm. 0.5			Three days after injection "papules all over body had disappeared"; eruption disappeared in 4 weeks; no relapse at end of 2½ months.		Weakly positive at the end of 9 wks.
43	F.	22	2	Macular syphilid.	One week.	None.	3/30/11, gm. 0.5	Arm sore two days; no nodules.		Macular eruption well at end of 1 month; one flat papule remains on knee; headache past 8 days; constipation relieved since injection.		Positive at the end of 4 weeks.
44	M.	21	2	Extensive mucous patches.	Six months.	Hg three weeks.	4/1/11, gm. 0.5		Chill, nausea.	Mucous patches disappeared in 24 hours; no relapse in 2 months.		Fatally positive at the end of 8 wks.
45	M.	24	3	Ulceration of lips.	One year.	Hg by mouth irregularly for 3 years.	4/1/11, gm. 0.5		Slight nausea.	Ulceration healed in 3 days; no relapse in 2 months.		Positive at the end of 8 weeks.
46	M.	30	3	Latent.		Hg by mouth intermittently for 5 years.	4/15/11, gm. 0.5		Severe chill, nausea; vomited three times; severe headache.	No new manifestations.		Weakly positive before treatment and at the end of 2 months.
47	M.	58	2	Miliary papular syphilid and iritis.	Eruption 3 mos., iritis 1 month.	24 injections.	4/25/11, gm. 0.5		Chill, nausea; vomited three times.	Eruption not quite disappeared in 8 weeks; iritis well in 3 weeks.		Positive at the end of 8 weeks.
48	F.	21	2	Papular syphilid.	Four months.	3 injections.	5/2/11, gm. 0.5		Headache for a few hours.	Eruption very slow to improve; still present at end of 6 weeks.		Negative in 4 wks.; weakly positive at the end of 6 wks.
49	F.	33	2	Small flat papular syphilid.	Two months.	Hg tablets 1 mo.	5/2/11, gm. 0.3			Eruption disappeared in 1 month.		
50	M.	33	3	Inchelpen labes.		Hg by mouth irregularly 10 years.	5/2/11, gm. 0.5		Chilly feeling; slight nausea.	No effect on symptoms.		
51	M.	9	2	Alopecia.	Six mos. since infection.	None.						Positive at the end of 6 weeks.
52	M.	48	3	Tubercular syphilid; leukoplakia.	Ten years, at times disappearing.	None.	5/4/11, gm. 0.5		Severe headache on following night.	Eruption disappeared at end of 5 weeks; temporary improvement in leukoplakia, <i>c. p.</i> softer and thinner but same area.		Negative in 5 and at end of 6 wks.
53	F.	30	2	Large flat papular syphilid; iritis (double).	Eruption 3 weeks, iritis 10 days.	None.	5/6/11, gm. 0.5			Double iritis well in 3 weeks; practically no change in eruption.		Strongly positive at end of 4 weeks.
54	M.	55	3	Tuberculo-squamous syphilid of foot.	Seven months.	Hg by mouth 3 years.	5/9/11, gm. 0.45			Eruption entirely disappeared at end of 4 weeks; pain in ankle stopped at end of 2 weeks; no relapse at end of 3 months.		Negative at the end of 5 weeks.
55	F.	19	2	Latent.	Two mos. since infection.	Hg by mouth 6 weeks.	5/11/11, gm. 0.5			No manifestations at the end of 5 weeks.		Weakly positive at the end of 4 wks.
56	M.	42	2	Ulceration base tongue; hyperemia of larynx.	Eighteen months.	Hg by mouth 18 months.	5/11/11, gm. 0.4	Vein obliterated by induration one inch long, size of a goose quill.	Nausea; vomited twice.	When seen 1 month later the lesions had entirely disappeared.		Negative at the end of 1 weeks.
57	F.	37	2	Mole papules; specific acrodermatitis.		Hg by mouth 1 year.	5/13/11, gm. 0.4	One pea-sized nodule lasting four days; vein partially obliterated.	Chill, nausea; vomited four times; severe headache.	Mole papules healed in 6 days; papule at corner of mouth in 2 days; negro reticulae practically well at end of 3 weeks (see text).		Weakly positive at the end of 4 wks.
58	M.	27	3	Verrucous syphilid, both palms and soles.	Two years.	Hg by mouth and injections for 18 mos., 2½ years ago; Hg for 2 mos. by mouth and injection, since lesions appeared; very slight result.	5/13/11, gm. 0.5		Slight chill, nausea; vomited five times; slight headache.	Both palms entirely well at the end of 1 week; both soles entirely well at the end of 1 month.		Fatally positive at the end of 4 wks.
59	F.	20	2	Corymbiform papular syphilid.	Four and one-half months.	None.	5/13/11, gm. 0.5	One nodule, size of large pin-head, lasting 2 weeks.	Chill, nausea; vomited once; slight headache.	Eruption began to improve on second day, disappearing at the end of 1 month.		Positive before treatment; strongly positive at end of 3 weeks.
60	M.	27	2	Mucous patches.	Two months.	None.	5/18/11, gm. 0.5		Vomited once.	Mucous patches disappeared in 2 days.		Positive at the end of 3 weeks.
61	M.	44	3	Latent.		3 mos. ago salvarsan given subcutaneously; an ulcerated leg of 10 years' duration had then healed.	5/19/11, gm. 0.5					Strongly positive at the end of 4 wks.
62	M.	47	2	Iritis.	One week.	None.	5/20/11, gm. 0.5			Iritis practically well at end of 3 weeks.		
63	M.	36	2	Papular syphilid; kerato-iritis.	Iritis one week.	None.	5/20/11, gm. 0.5			Slight improvement in one eye up to fourth day, when iritis developed in other eye; iritis greatly improved at end of 3 weeks.		Weakly positive at the end of 3 wks.
64	F.	19	1	Chancre of lip; local adenopathy.	Three weeks.	None.	5/21/11, gm. 0.5		Chill, nausea; vomited four times; severe headache.	Chancre covered with epidermis on fourth day; greatly lessened in size at end of 2 weeks; glands somewhat smaller; no other manifestations have appeared.		Fatally positive at the end of 3 wks.
65	M.	47	3	Tubercular syphilid of cheek and lip.	Two years.	None.	5/22/11, gm. 0.5			Eruption began to improve on second day and was almost imperceptible at end of 10 days.		

* 1, primary; 2, secondary; 3, tertiary.

† Hereditary.

TABLE 4.—PATIENTS TREATED WITH ONE INTRAMUSCULAR INJECTION (OILY SUSPENSION)

Case No.	Sex	Age	Stage	Lesions	Duration of Lesions	Previous Treatment	Date and Dosage	Local Effect of Injection	Clinical Result	Remarks	Wassermann Reaction
60 F.	10	1	1	Gummatous ulceration of nose.	Four years.	Hg internally 1 month.	2/5/11, gm. 0.4	Pain and induration moderate.	Moderate improvement at end of 1 month; later severe 3 more injections by another physician and lesions healed after second injection.	Positive at the end of 3 weeks.	
67 F.	34	2	1	Miliary papular syphilis.	Three months.	None.	2/13/11, gm. 0.5	Severe pain and lameness.	Eruption about to disappear; not entirely gone end of 2 months; patient given 10 mg. of 2% ephedrine.	Negative at the end of 4 wks.	
68 F.	45	3	1	Tuberculo-syphilis of nose.	Twelve years.	Hg by mouth intermittently for 6 years.	3/9/11, gm. 0.5	Pain two weeks; induration moderate.	Eruption disappeared entirely at end of 1 month; no relapse at end of 3 months (toxic erythema on seventh day; see text).	Negative 1 month; positive at the end of 3 months.	
69 F.	22	2	1	Miliary syphilis.	Six weeks.	None.	3/14/11, gm. 0.5	Not much pain; lameness for 2 wks.	Pain in joints disappeared in 1 week; eruption well in 10 days.	Negative at the end of 6 wks.	
70 F.	28	3	1	Latent.	Hg for 1 year by mouth and injections.	3/19/11, gm. 0.4	Pain and induration for a week in spite of remaining in bed; necrosis at end of five weeks.	Faintly positive at the end of 2 weeks.	
71 M.	26	2	1	Latent.	Small amount Hg by mouth and injections.	3/29/11, gm. 0.5	Pain considerable for a week; moderate induration; no lameness.	Gained 4 pounds in 3 months.	Negative at the end of 10 wks.	
72 M.	31	3	1	Ulceration of mouth; leukoplakia.	Hg by mouth irregularly nine years.	3/29/11, gm. 0.5	Severe pain and induration; very little relief for 2 weeks; Hg still at end of one month.	Ulceration of mouth healed in 2 days; no effect on leukoplakia.	Positive at the end of 4 weeks.	
73 M.	51	3	1	Recurring patches.	Three years.	Hg by mouth 3 months.	4/1/11, gm. 0.5	Severe pain, induration and lameness lasting 3 weeks.	One mucous patch disappeared in 1 day; another in 3 days.	Negative in 3 and 9 wks.	
74 F.	23	3	1	Tuberculo-syphilis of nose.	Three years.	None.	4/1/11, gm. 0.5	Pain and induration severe; lameness for two weeks.	Eruption disappeared completely in 3 weeks; pustules disappeared entirely; gained 15 pounds in 1 month.	Positive at the end of 4 weeks.	
75 F.	43	3	1	Latent.	Hg for many yrs. by mouth and few injections.	4/19/11, gm. 0.5	Pain, induration and lameness 2 weeks; confined to bed one week.	Gained 10 pounds since injection.	Faintly positive at the end of 7 weeks.	
76 F.	36	3	1	Tubercular syphilis of cheek.	One year.	None.	4/21/11, gm. 0.5	Severe pain and induration; in bed 2 weeks.	Eruption began to improve on third day and lesions detached at end of 2 weeks; only slight skin left at end of 6 weeks.	Strongly positive at the end of 4 weeks.	
77 F.	27	3	1	Tubercular syphilis of both palms; plantar syphilis of feet.	One month.	None.	5/15/11, gm. 0.5	Severe pain; lameness for five days.	Eruption of palms entirely well at end of a month; no effect on plantar syphilis.	Strongly positive at the end of 4 weeks.	
78 F.	29	3	1	Tubercular syphilis of feet.	Seven years.	None.	5/16/11, gm. 0.5	Severe pain, induration and lameness for 2 weeks.	Eruption began to improve on second day; at end of 2 weeks lesions entirely the end of 3 weeks; partial relapse at end of 4 weeks.	Positive at the end of 3 weeks.	
79 F.	25	2	1	Large flat nodular syphilis.	None.	5/24/11, gm. 0.5	Pain for one week; induration moderate.	Eruption began to disappear on second day; satisfactory improvement at end of 10 weeks.	Positive at the end of 3 weeks.	

* 1, primary; 2, secondary; 3, tertiary.
† Hereditary.

TABLE 5.—PATIENTS TREATED WITH MULTIPLE INJECTIONS

Case No.	Sex	Age	Stage	Lesions	Duration of Lesions	Treatment	Date, Method and Dosage of Injection	Local Effect of Injection	General Effect of Injection	Clinical Result	Remarks
80 M.	19	2	1	Pustulo-crumbly syphilis of arms, legs and ear.	Eight months.	Hg by mouth for 3 months.	10/15/10, subcutaneous gm. 0.4; 12/25/10, intramuscular gm. 0.45 (alkaline solution); 1/21/11, intramuscular gm. 0.5 (alkaline solution); 3/9/11, intramuscular gm. 0.5 (oil).	Pain 1 day and slight induration from first injection; practically no pain or induration from second; arm sore for 2 days following intravenous injection (see text); no pain or induration from last injection.	Ulcers of leg healed at end of 1 month; ulcers of nose and arm markedly improved at end of 3 weeks; then relapsed; after second injection improvement for a week; stationary for 2 weeks; then slight relapse; after third injection arm healed in 1 week and nose in 10 days; slight relapse of arm at end of 2 1/2 weeks; 1 month after last injection took 10 mg. of 2% ephedrine for 3 weeks and suffered slight relapse while under treatment; gained 12 pounds.	Faintly positive after third injection; strongly positive at the end of 8 months.	
81 F.	20	2	1	Miliary syphilis.	Six days.	None.	10/22/10, subcutaneous gm. 0.45; 1/26/11, intramuscular gm. 0.6 (alkaline solution).	Pain and induration moderate after first injection; induration persisted at end of 8 months; severe pain and induration after second injection.	Eruption disappeared in 4 weeks; severe relapse at end of 6 1/2 weeks; relapse of mucous patches of mouth and vulva and a macule on face; pustules disappeared 3 wks. after second injection and at end of 10 weeks again relapsed in the form of a papular syphilis.	Strongly positive at the end of 8 months.	
82 F.	20	2	1	Papular syphilis.	Three weeks.	None.	10/28/10, subcutaneous gm. 0.4; 12/25/10, intramuscular gm. 0.3; 3/4/11, intramuscular gm. 0.5 (oil).	Pain and induration slight after first injection; no pain or induration after second injection; considerable pain and induration after third injection.	Eruption nearly well at end of 2 months, when she had gained 10 pounds; 1 month later pain in thighs and perineals of both thighs; pain in thigh stopped on second day and healed on third day after intravenous injection.	Negative in 5 weeks after first injection; positive at the end of 4 1/2 mos.	
83 M.	38	3	1	Ulceration of hard and soft palate.	Six months.	Hg by mouth, injections and injections for one year; Hg very badly borne.	11/10/10, intramuscular gm. 0.5 (alkaline solution); 12/15/10, intramuscular gm. 0.6 (alkaline solution).	Pain 2 days; no induration after first injection; no pain or induration at all after second injection.	Ulceration of palate nearly healed at end of 2 weeks; relapsed 1 week later; began to improve 10 days after second injection and entirely healed at end of 2 months; great improvement in general health; no further relapse at end of 7 months; gained 20 pounds (see text).	Negative in 5 weeks and at the end of 7 months.	
84 M.	40	3	1	Lepa tuberculous.	Six years.	1/3/11, intramuscular gm. 0.5 (alkaline solution); 3/30/11, intramuscular gm. 0.5 (oil).	Severe pain for 8 days and moderate induration after first injection.	Severe ulceration for a week after first injection.	Marked improvement in ulcerated lesions at end of 3 weeks; partial relapse at end of 4 weeks; no effect on solid nodular lesions; no change noticed after intravenous injection (see text).
85 F.	32	3	1	Gummatous ulceration of nose.	Nine months.	Hg by mouth 4 1/2 weeks.	4/12/11, intramuscular gm. 0.5 (alkaline solution); 3/30/11, intramuscular gm. 0.5 (oil).	Pain for 1 day; no induration after first injection; considerable pain and induration after second injection.	Ulceration healed in 3 weeks; slight relapse 1 week later; 1 week after second injection discharge stopped and lesions healed; no further relapse at end of 5 months; gained 17 pounds; herpes zoster on fourth day after second injection.	Positive at the end of 5 months.	
86 M.	26	3	1	Perforitis of tibia.	Three years.	Hg by injections intermittently 4 years.	10/19/10, intramuscular gm. 0.5 (oil); 3/28/11, intramuscular gm. 0.6 (alkaline solution).	No pain or induration after first injection; severe pain for 3 days; induration 10 weeks after second injection.	Pain and tenderness of tibia stopped entirely on second day; free of pain for 5 weeks; then it returned; symptoms again relieved after second injection, but returned again in original severity; both injections relieved pain better than injections of mercury.	Negative in 8 weeks and at the end of 3 months.	
87 F.	23	2	1	Larce flat papular syphilis.	Seven months.	Hg by mouth 7 weeks with Hg effect.	4/19/11, intramuscular gm. 0.45 (oil); 3/4/11, intramuscular gm. 0.45.	No pain or induration after first injection.	Nausea; vomiting three times after intramuscular injection.	Very slow improvement after both injections; eruption practically well at end of 6 months.	Faintly positive at the end of 6 months.
88 F.	10	2	1	Miliary syphilis.	One week.	None.	1/26/11, intramuscular gm. 0.5 (oil); 3/9/11, intramuscular gm. 0.5.	Pain 3 days; induration moderate; slight pustule at end of 1 week, discharging about end of 4 1/2 mos.	No reaction after intravenous injection.	Eruption disappeared at end of 1 week; relapsing miliary syphilis on fifth day, disappearing 1 week after second injection; no further relapse at end of 4 1/2 months.	Faintly positive at the end of 4 1/2 mos.
89 M.	20	2	1	Pustulo-crumbly syphilis of nose.	Six weeks.	None.	1/26/11, intramuscular gm. 0.5 (oil); 2/1/11, intramuscular gm. 0.5.	No pain or induration from first injection.	Slight headache after intravenous injection.	Slight improvement at end of 1 week; lesion healed 1 month after second injection; gained 7 pounds; no relapse at end of 3 1/2 months.	Faintly positive in 2 weeks and at the end of 4 1/2 months.
90 F.	53	2	1	Miliary syphilis; postititis.	10 weeks, isolated 40 years.	None.	3/4/11, intramuscular gm. 0.5 (oil); 3/9/11, intramuscular gm. 0.5 (oil).	Pain, severe; confined to bed for a week after second injection.	Chill, nausea; vomiting three times after intravenous injection.	Miliary syphilis disappeared in about a month; postititis healed in 10 weeks (see text).	Faintly positive at the end of 3 months.
91 M.	41	3	1	Latent.	Nineteen years since first infection; 19 injections before.	Hg by mouth 5 years; first, recently 19 injections.	5/5/11, intramuscular gm. 0.5 (oil); 5/11/11, intramuscular gm. 0.5 (oil); 5/20/11, intramuscular gm. 0.5.	Severe induration and lameness for a week after intramuscular injection.	Chills, fever, nausea; vomiting three times after first injection; no reaction after second intravenous injection.	For a week following each injection severe headache (from which he had suffered for several months), lessened and then disappeared; they were, however, much less severe than before the injections; gained 20 pounds; 3 weeks after last injection put on mercurial treatment.	Strongly positive at the end of 3 months.
92 M.	24	3	1	Superficial ulceration of tongue.	Two months.	Hg by mouth 13 months.	13/28/11, intramuscular gm. 0.5; 4/8/11, intramuscular gm. 0.5 (oil); 5/20/11, intramuscular gm. 0.5.	Soreness and lameness for 2 weeks after intramuscular injection.	Chill; vomiting three times; severe headache after second injection; no reaction after third injection.	Ulceration of tongue healed in 5 days; no relapse at end of 2 1/2 months.	Weakly positive at the end of 2 1/2 mos.
93 M.	17	1	1	Chancre of lip.	Three weeks.	None.	3/27/11, intramuscular gm. 0.5; 4/1/11, intramuscular gm. 0.5 (oil).	Practically no pain or induration after intramuscular injection.	Slight chill, nausea; vomiting three times; slight headache after intramuscular injection.	Chancre covered with epidermis in 5 days; 1 week after second injection put on mercurial treatment.
94 M.	34	3	1	Tuberculo-syphilis of nose and face.	Lesions of nose, two years; of face, ten years.	Practically none.	1/15/11, intramuscular gm. 0.5; 3/9/11, intramuscular gm. 0.5 (oil).	Odorization of nose, but no nodules after intramuscular injection; lameness for 3 days after intramuscular injection.	No reaction after first injection; slight reaction after second intravenous injection.	Slight improvement in eruption at end of 2 weeks; eruption for several days stopped at end of 2 days; lesions entirely healed 2 weeks after second injection; no relapse at end of 2 months.	Positive at the end of 2 months.
95 M.	35	3	1	Latent.	Cont years since infection.	Hg by mouth 3 years; regularly 3 years.	4/15/11, intramuscular gm. 0.5; 4/21/11, intramuscular gm. 0.2.	No pain or induration after first injection.	No symptoms after either injection.	No clings at end of 2 months.
96 M.	30	3	1	Severe head aches, not thoroughly controlled by Hg.	Eight years since infection.	Hg by mouth 3 years.	2/1/11, intramuscular gm. 0.45; 5/9/11, intramuscular gm. 0.5.	Chill and nausea after first injection; throat dry for 2 weeks; less severe chill and slight headache after second injection.	Chills and nausea after first injection; throat dry for 2 weeks; less severe chill and slight headache after second injection.	Headaches disappeared on second day after first injection; no relapse at end of 7 weeks.	Weakly positive at the end of 7 weeks.
97 F.	128	3	1	Latent.	Eight years since infection.	Hg by mouth 20 injections.	4/22/11, intramuscular gm. 0.5 (oil); 5/20/11, intramuscular gm. 0.5.	No pain, but slight induration after intramuscular injection; pain, but no nodules after intravenous injection.	Severe chill, nausea; vomiting three times after first injection; no reaction after second intravenous injection.	New lesions (thierules) developed on hands 1 week after first injection; disappeared 5 days after second injection; 10 days later perforated nodules of forehead developed.	Negative at the end of 3 wks.
98 F.	41	3	1	Extensive syphilis of skin, arms and neck.	Three years.	None.	4/22/11, intramuscular gm. 0.5; 2/3/11, intramuscular gm. 0.5; 5/11/11, intramuscular gm. 0.5 (oil).	Slight soreness, no induration after intramuscular injection.	Nausea; vomiting twice; chill after first intravenous injection; no reaction after second and third intravenous injections.	Crusts began to fall at end of 1 week and at end of 6 weeks lesions entirely smooth; have grown steadily better and paler in the course of 10 weeks.	Strongly positive at the end of 5 weeks.
99 F.	34	3	1	Gummatous ulceration of knee.	One year.	"Pills and drops for a year."	7/27/11, intramuscular gm. 0.45; 5/4/11, intramuscular gm. 0.12.	Pain, induration but no nodules after first injection.	Chill; frequent vomiting; head aches; fever and slight headache after second injection.	Ulcers healed at end of 10 weeks; menstruation less profuse since injection.	Faintly positive at the end of 4 weeks.
100 F.	22	3	1	Gummatous ulceration of knee.	Two years.	None.	7/4/11, intramuscular gm. 0.1; 5/4/11, intramuscular gm. 0.5 (oil).	One bean-sized nodule after first injection; disappeared in 1 day; no induration of vein; pain severe, induration moderate after intramuscular injection.	Slight chill; fever and nausea after intravenous injection.	Ulcers entirely healed at end of 1 month; pain in knee stopped at end of 1 week; menstruation always regular, but more so since treatment; no relapse at end of 6 weeks.	Strongly positive at the end of 4 weeks.

* 1, primary; 2, secondary; 3, tertiary.

Hereditary.

8. The intramuscular and intravenous methods of administration are probably of equal efficiency.

9. The intravenous method is the one of choice where rapidity of action and the comfort of the patient are factors to be considered.

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